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Patent Application
Attorney Docket No.PC11724D

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By Kelly A Smith
(Signature of person mailing)
Kelly A. Smith
(Typed or printed name of person)

THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Zheng J. Li, et al.

APPLICATION NO.: 10/650,253 : Examiner: PESELEV, ELLI

FILING DATE: August 27,2003 : Group Art Unit: 1623

TITLE: CRYSTAL FORMS OF AZITHROMYCIN

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY BRIEF

This Reply Brief is being filed under 37 C.F.R. §41.41(a)(1) and §41.43(b) in response to the Examiner's Answer dated August 31 to further clarify Applicants' positions and to rebut the Examiner's assertions.

The due date for a Reply Brief is October 30, 2006. Therefore, the present Reply Brief is being timely filed.

EXPRESS MAIL NO. EV713244093US

STATUS OF CLAIMS

1. Claims 125 and 128-144 are pending and currently under appeal. Claims 1-124 and 126-127 have been canceled without prejudice.

2. Claims 125 and 128-144 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

3. Claims 125 and 128-144 have been rejected under 35 U.S.C. §102(b) as being anticipated by Bright, U.S. Patent No. 4,474,768.

4. Claims 125 and 128-144 have been rejected under 35 U.S.C. §103(a) as being obvious over Bright, U.S. Patent No. 4,474,768.

5. Claims 125 and 128-144 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Singer et al., U.S. Patent No. 6,365,574 in view of Curatolo et al., U.S. Patent No. 5,605,889.

6. No claims have been allowed.

GROUNDS OF REJECTIONS TO BE REVIEWED ON APPEAL

I. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 USC §112, first paragraph, as failing to comply with the enablement requirement

II. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Bright, U.S. Patent No. 4,474,768 ("Bright").

III. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 U.S.C. §103(a) as being unpatentable over Singer et al., U.S. Patent No. 6,365,574 ("Singer") in view of Curatolo et al., U.S. Patent No. 5,605,889 ("Curatolo").

ARGUMENTS

I. Rejection of Claims 125 and 128-144 Under 35 U.S.C. §112, First Paragraph, as failing to comply with the enablement requirement

Applicants respectfully point out that the Examiner's assertion that these claims include "aqueous azithromycin solutions" is contrary to the case laws and contrary to the clear language of the claims as well as Applicants' unambiguous statements in file history. In addition, the Examiner failed to respond to Applicants' contention that the Examiner arbitrarily rejected these claims.

THE EXAMINER'S ASSERTION IS CONTRARY TO THE CASE LAWS AND TO THE CLEAR LANGUAGE MEANING OF THE CLAIMS

The Examiner's only assertion with regard to this rejection is that these claims have to be interpreted to include aqueous azithromycin solutions because page 32 of the specification, lines 32-33 stated that carriers include sterile aqueous media. Such an assertion is contrary to the case laws and the public policy which encourage applicants to dedicate the subject matter that is disclosed but not claimed, to the public. As the Federal Circuit Court stated in *Maxwell v. J. Baker, Inc.*, 939 F.2d 1558, 1562-63 (Fed. Cir. 1991) that "we reiterated the well-established rule that 'subject matter disclosed but not claimed in a patent application is dedicated to the public'" and that an applicant could "present a broad disclosure in the specification of the application and file narrow claims," thereby "avoiding examination of broader claims that the applicant could have filed consistent with the specification." *Id* at 1107.

In this case, Applicants followed the exact holding of the Federal Circuit Court in *Maxwell v. J. Baker, Inc.* and presented a broad disclosure of the pharmaceutical dosage form which includes aqueous azithromycin solutions but filed narrow claims which exclude aqueous azithromycin solutions by defining the claimed subject matter as "having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm." Such claim language would exclude aqueous azithromycin solutions from the claimed pharmaceutical dosage form because it has not been known in the art that ^{13}C solid state NMR spectrum can be detected/measured for an aqueous azithromycin solution. Applicants presented such claims to avoid examination of broader claims that would have covered

aqueous azithromycin solutions as stated by the Federal Circuit Court in *Maxwell v. J. Baker, Inc.*, thereby saving time and expenses of the Applicants, the Examiner and this Board. In addition, Applicants have made unambiguous statements in the file history that these claims do not cover aqueous azithromycin solution and "[S]uch intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

Applicants respectfully submit that the Examiner is simply wrong by not following the Federal Circuit Court holdings in *Maxwell v. J. Baker, Inc.* and in *Vitronics Corp. v. Conceptronic, Inc.* and by examining broad claims that are not actually presented. Therefore, Applicants respectfully request that this ground of rejection be reversed.

THE EXAMINER ARBITRARILY REJECTED THESE CLAIMS

Federal Circuit Court holdings and claim interpretation aside, the Examiner could still have withdrawn this ground of rejection by entering an amendment to the specification to delete the reference to "sterile aqueous media" on page 32 so as to obviate an appeal to this rejection and to other grounds of rejections in this case. As a practical matter, doing so would have saved time and expenses of the Applicants, the Board and the Examiner.

It is also worthwhile to note that the Examiner's position in this application is contrary to those taken in recent cases. To support such an assertion, Applicants would like to direct the Board's attention to U.S. Patent No. 6,936,591 ("the '591 patent"). The following table directly compare the '591 patent and the present application.

	The '591 patent	The present application
Primary Examiner	Elli Peselev	Elli Peselev
Patentees/Applicants	Dumic et al.	Li et al.
Assignee	Pliva Pharmaceutical	Pfizer, Inc.
Issue/Final Rejection Dates	August 30, 2005	March 16, 2006
Pharmaceutical composition claims	Claim 32	Claims 125 and 128-144 with claim 125 as the independent claim
Drug crystals in the claimed pharmaceutical composition/ pharmaceutical dosage form	Substantially pure orthorhombic isostructural pseudopolymorph of 9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin A (azithromycin)	Substantially pure azithromycin monohydrate hemi-isopropanol solvate
Claim element that would exclude "an aqueous azithromycin solution"	None	having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm
Specification on the use of aqueous solvent as an excipient/carrier	See Col. 11, lines 28-31 for "oral solution"; see Col. 12, lines 48-53 for "sterile aqueous solution";	Page 32, lines 32-33 listed the phrase "sterile aqueous media"
Unambiguous statements on the scope of the claims to exclude aqueous azithromycin solutions	None	Repeated numerous times during the prosecution and during this appeal
Proposed amendment to delete reference to sterile aqueous solution/media	None	Requested
Status	Issued	Finally rejected and currently on appeal

Applicants note that both the '591 patent and the present application have the same Examiner. The '591 patent claimed a pharmaceutical composition containing orthorhombic isostructural azithromycin while the present application claims pharmaceutical dosage form containing azithromycin monohydrate hemi-ethanol solvate. The '591 patent included the term "sterile aqueous solution" and the present application included the term "sterile aqueous media" in the descriptions of carriers/excipients.

There are two major differences between these two cases in favor of allowing the

present application. One is the claims of the present application define the claimed subject matter as "having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm" which exclude "an aqueous azithromycin solution" while the '591 patent is silent on this. The other is Applicants in the present case made unambiguous statements in the file history that these claims do not cover "aqueous azithromycin solutions" while the '591 patent is silent on this.

Based on these facts, one would expect that the present application should be at least allowed in the same way as the '591 patent. After all, the '591 patent was issued on August 30, 2005 without any limitation to exclude "aqueous azithromycin solution" and without any statement to such effect in the file history. Less than 7 months later, the same Examiner finally rejected the present claims as "including aqueous azithromycin solution" when the clear language of the claims and the file history indicate the opposite. In the absence of an explanation for doing so, Applicants respectfully submit that the Examiner was simply making arbitrary decisions on what is patentable and what is not.

To reinforce the notion that the Examiner has been making arbitrary decisions, Applicants would like to point out that on July 29, 2003, Examiner Elli Peselev issued U.S. Patent No. 6,599,884 ("the '884 patent") to Avrutov et al. of Teva Pharmaceutical Industries, Ltd. wherein its claim 14 is directed to a pharmaceutical composition comprising a therapeutically effective amount of clarithromycin Form IV. Applicants note that in Column 7, lines 31-36 of the '884 patent, the patentees described "liquid dosage form" that contains "water." In allowing the issuance of the '884 patent, the Examiner followed the same standard as that of the '591 patent. Applicants respectfully conclude that the Examiner used one patentability standard from July 29, 2003 to August 30, 2005 to allowed the '884 patent and the '591 patent to issue and then adopted a different standard on March 16, 2006 to finally reject the claims of the present application. Based on this type of arbitrary decisions alone, Applicants respectfully request that the Board reverse this ground of rejection or reverse this rejection with the condition that the present specification be amended to delete the reference to "sterile aqueous media" on page 32.

II. Rejection Of Claims 125 And 128-144 Under 35 U.S.C. §102(b) As Being Anticipated By Or, In The Alternative, Under 35 U.S.C. §103(a) As Obvious Over Bright, U.S. Patent No. 4,474,768 ("Bright")

Applicants would like to point out that these grounds of rejections are based on the Examiner's assertion that claims 125 and 128-144 include aqueous solutions of azithromycin. As stated in Applicants' reply to the same assertion in Examiner's Answer in rejection under 35 U.S.C. §112, first paragraph, Applicants believe that such an interpretation is contrary to the case laws and the public policy which encourage applicants to dedicate the subject matter that is disclosed but not claimed, to the public. As the Federal Circuit Court stated in *Maxwell v. J. Baker, Inc.*, 939 F.2d 1558, 1562-63 (Fed. Cir. 1991) that "we reiterated the well-established rule that 'subject matter disclosed but not claimed in a patent application is dedicated to the public'" and that an applicant could "present a broad disclosure in the specification of the application and file narrow claims," thereby "avoiding examination of broader claims that the applicant could have filed consistent with the specification." *Id* at 1107.

In this case, Applicants followed the exact holding of the Federal Circuit Court in *Maxwell v. J. Baker, Inc.* and presented a broad disclosure of the pharmaceutical dosage form which includes aqueous azithromycin solutions but filed narrow claims which exclude aqueous azithromycin solutions by defining the claimed subject matter as "having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm." Such claim language would exclude aqueous azithromycin solutions from the claimed pharmaceutical dosage form because it has not been known in the art that ^{13}C solid state NMR spectrum can be detected/measured for an aqueous azithromycin solution. Applicants presented such claims to avoid examination of broader claims that would have covered aqueous azithromycin solutions as stated by the Federal Circuit Court in *Maxwell v. J. Baker, Inc.*, thereby saving time and expenses of the Applicants, the Examiner and this Board. In addition, Applicants have made unambiguous statements in the file history that these claims do not cover aqueous azithromycin solution and "[S]uch intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

Applicants respectfully submit that the Examiner is wrong not to follow the Federal Circuit Court holdings in *Maxwell v. J. Baker, Inc.* and in *Vitronics Corp. v. Conceptronic, Inc.* and not to examine the claims that were actually presented. Applicants respectfully

submit that claims 125 and 128-144, as actually presented by Applicants, are neither anticipated nor rendered obvious by Bright. Therefore, reversal of these rejections are respectfully requested. Alternatively, these rejections should be reversed with the entry of an amendment to the specification to delete the term "sterile aqueous media" from page 32 of the specification.

III. Rejection of Claims 125 and 128-144 under 35 U.S.C. §103(a) as Being Unpatentable Over Singer et al., U.S. Patent No. 6,365,574 ("Singer") in view of Curatolo et al., U.S. Patent No. 5,605,889 ("Curatolo")

Applicants would like to point out that the Examiner's Answer is silent as to Applicants' contention that a combination of azithromycin ethanol solvate with MIGLYOL 812 is a dosage form and it may be taken as an admission by the Examiner that she was incorrect on this issue.

THE DECLARATION OF RICHARD TODD DARRINGTON IS SUFFICIENT TO REMOVE SINGER AS A REFERENCE

The Examiner's Answer asserted regarding Dr. Richard Todd Darrington's declaration, that "This argument has not been found persuasive because a declaration under 37 C.F.R. §1.131 is not sufficient where the reference is a domestic patent which is claiming a substantially the same invention as the appellant."

Applicants respectfully contend that the Examiner's assertion is also incorrect because Singer does not claim substantially the same invention as the present application. Specifically, Singer did not teach any pharmaceutical dosage form comprising substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate and a pharmaceutically acceptable carrier or diluent; wherein said crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm. Nor did Singer teach any pharmaceutical dosage form with the advantages of having desirable tablet tensile strength of over 1.5 MPa. *see the Rule 132 declaration by Dr. Bruno C. Hancock filed in the present application on August 29, 2005.* As further support of Applicants' contention, the Examiner also admitted on record that Singer alone or Curatolo alone would not anticipate claims 125 and 128-144 nor render these claims obvious. The Examiner actually alleged that the

combination of Singer and Curatolo render these claims obvious.

As Singer alone does not anticipate these claims nor render them obvious, the issue of whether the declaration of Richard Todd Darrington is sufficient to remove Singer as a reference is moot because Singer alone could not have taught substantially the same subject matter as those of claims 125 and 128-144 by the Examiner's own admission. Therefore, this ground of rejection must be reversed.

THE EXAMINER'S ASSERTION IS WRONG

The Examiner asserted that "Appellant further contends that a pharmaceutical dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate is unexpected. This argument has not been found persuasive since no verified evidence of unexpected results has been presented for consideration." The Examiner is simply wrong on this, again. On August 29, 2005, Applicants filed a Rule 132 declaration of Dr. Bruno C. Hancock with tableting performance data showing that among the five different kinds of tablets containing various types and amount of azithromycin polymorphs, only tablets with substantially pure azithromycin monohydrate hemi-ethanol solvate achieved a tensile strength higher than the desired 1.5MPa. All other four tablets, including one containing about 51% azithromycin ethanolate, have tensile strength of less than 1.0 MPa. Moreover, Applicants have made the pharmaceutical dosage form in such a way that a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm can be measured/detected.

In the face of such glaring evidence of superior/unexpected properties of the claimed subject matter from the specification, the claims and the 132 declaration, it is simply wrong for the Examiner to state that no evidence of unexpected results was ever presented. As a matter of fact, the 132 declaration was filed in August 2005, the claims on appeal were before the Examiner at the time of the Examiner's Answer and the original specification has been on file for several years. When such "unexpected results" are given due weight under the Federal Circuit Court's holding in *In re Sernaker*, 702 F.2d 989, 217 (Fed. Cir. 1983), this ground of rejection must be reversed.

CONCLUSION

For the foregoing reasons Applicants respectfully request that all rejections of claims 125 and 128-144 be reversed.

It is believed that no fee is deemed necessary in connection with the filing of the present Reply Brief. However, if any fees are required, the Board is hereby authorized to charge any such fees to our Deposit Account No. 16-1445.

Respectfully submitted,

Date: 09/13/06

Lance Liee

Lance Y. Liu
Attorney for Applicant(s)
Reg. No. 45,379

Customer No. 28523
Pfizer Inc.
Patent Department, MS 8260-1611
Eastern Point Road
Groton, Connecticut 06340
(860) 686-1652